

FACSIMILE COVER SHEET

CONFIDENTIAL AND PRIVILEGED

Perkins
Coie

101 Jefferson Drive
Menlo Park, CA 94025-1114
PHONE: 650.838.4300
FAX: 650.838.4350
www.perkinscoie.com

DATE: April 21, 2004 COVER SHEET & 11 PAGE(S)ORIGINAL DOCUMENT(S) WILL BE: ☐ SENT TO YOU ☒ HELD IN OUR FILES

SENDER:	TELEPHONE:	FACSIMILE:
LeeAnn Gorthey	650-838-4403	650-838-4350

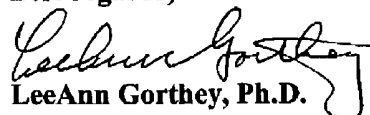
RECIPIENT:	COMPANY:	TELEPHONE:	FACSIMILE:
Examiner J. Epps-Ford	USPTO Art Unit 1635	(571) 272-0757	(571)273-0757

RE: US Serial No. 09/826,519
Atty Docket No. 1565.006 (52456.8017.US01)
and parent appn. US Serial No. 09/648,254, now U.S. Patent No. 6,677,445

Dear Examiner Epps-Ford,

Enclosed are copies of the restriction requirement made in US Serial No. 09/648,254 (made by telephone on 4/2/01 and reported in the Office Action dated 4/26/01; 5 pages enclosed) and the response submitted on 4/2/01 (6 pages).

Best regards,



LeeAnn Gorthey, Ph.D.

Patent Agent

Perkins Coie LLP

Reg. No. 37,337

This Fax contains confidential, privileged information intended only for the intended addressee. Do not read, copy or disseminate it unless you are the intended addressee. If you have received this Fax in error, please email it back to the sender at perkinscoie.com and delete it from your system or call us (collect) immediately at 650.838.4300, and mail the original Fax to Perkins Coie LLP, 101 Jefferson Drive, Menlo Park, CA 94025-1114.

ANCHORAGE · BEIJING · BELLEVUE · BOISE · CHICAGO · DENVER · HONG KONG · LOS ANGELES
MENLO PARK · OLYMPIA · PORTLAND · SAN FRANCISCO · SEATTLE · SPOKANE · WASHINGTON, D.C.
Perkins Coie LLP (Perkins Coie LLC in Illinois)


UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

 Address: COMMISSIONER OF PATENTS AND TRADEMARKS
 Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/648,254	08/25/00	INNIS	M 2456-0017.30

027476

HM22/0426

 Chiron Corporation
 Intellectual Property - R440
 P.O. Box 8097
 Emeryville CA 94662-8097

EXAMINER

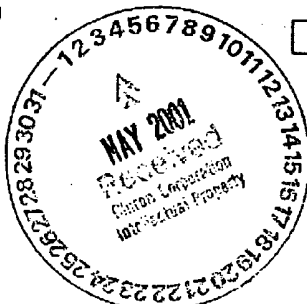
NGUYEN, L

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 04/26/01



Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

5/3/01, on
 DPL
 PP 01565.002
 RS3 7/26/01
 RS0 10/26/01

Non-Final Rejection of Restriction

Checked w/ USPTO and we do receive 3 mos
 not just 1 mo

Office Action Summary

Application No.

09/648,254

Applicant(s)

INNIS ET AL.

Examiner

Lauren Nguyen

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9-15 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 9-15 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claims ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____
- 18) ☐ Interview Summary (PTO-413) Paper No(s) ____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

APPLIC-IT

Application/Control Number: 09/648,254
Art Unit: 1635

Page 2

DETAILED ACTION

NON-FINAL

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-8, drawn to a chimeric oligonucleotide, classifiable in class 536, subclass 24.5, for example.
 - II. Claims 9-15, drawn to a composition comprising the chimeric oligonucleotide recited in Group I and a lipid-cationic peptoid conjugate of the formula: L-linker-
 $[N(CH_2CH_2NH_2)CH_2(C=O)-N(CH_2CH_2R)CH_2(C=O)-N(CH_2CH_2R)CH_2(C=O)]_3-NH_2$, classifiable in class 436, subclass 71, for example.
 - III. Claims 16 and 17, drawn to a composition comprising the chimeric oligonucleotide recited in Group I and a lipid-cationic peptoid conjugate of the formula: $L-(CH_2)_n-(C=O)-[N(CH_2CH_2NH_2)CH_2(C=O)-N(CH_2CH_2R)CH_2(C=O)-N(CH_2CH_2R)CH_2(C=O)]_3-NH_2$, classifiable in class 436, subclass 71, for example.
 - IV. Claims 18-21, drawn to a method of inhibiting expression of a target gene in a subject comprising administering to a subject an amount of the chimeric oligonucleotide recited in Group I, classifiable in class 435, subclass 325, for example.

These inventions are distinct, each from the other because of the following reasons:

Invention I is related to inventions II and III as combination and subcombination, respectively. Inventions in this relationship are distinct if it can be shown that (1) the

Application/Control Number: 09/648,254
Art Unit: 1635

Page 3

combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the chimeric oligonucleotide can be used as DNA probes, obviating the use of a lipid-cationic peptoid conjugate. The subcombination has separate utility such as use as DNA probes, for example.

Inventions II and III are distinct, each from the other, because they are directed to materially different products. In this instance, the composition of group II comprises of a chemically distinct lipid-cationic peptoid conjugate from that of group III. The lipid-cationic peptoid conjugate of the two groups have different chemical formulas containing different lipid moieties; thus necessitating separate and distinct chemical considerations for examination. Therefore, the two inventions named above are directed to materially different products and would require a separate field of search.

Inventions I, II, and III are related to invention IV as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the chimeric oligonucleotide of I and the compositions containing a lipid-cationic peptoid conjugate of II and III can be used inhibition of gene expression *in vitro*, such as in cell culture studies for example.

Application/Control Number: 09/648,254
Art Unit: 1635

Page 4

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with Mr. David Lentini on April 2, 2001 a provisional election was made without traverse to prosecute the invention of group II, claims 9-15. Subsequent to such telephone conversation on April 2, 2001 with Mr. Lentini, a preliminary amendment was filed canceling all non-elected claims.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

I hereby certify that the following correspondence in being transmitted by facsimile to: Assistant Commissioner for Patents, Washington, D.C. 20231 on April 2, 2001
By: [Signature]

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Reinhard and Zuckermann, *et al.*

Serial No.: 09/648,254

Filed: August 25, 2000

Title: CHIMERIC ANTISENSE OLIGONUCLEOTIDES
AND CELL TRANSFECTING FORMULATIONS
THEREOF

Examiner: Nguyen, L.

Art Unit: 1635

**RESPONSE TO RESTRICTION
REQUIREMENT AND AMENDMENT A**The Honorable Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Responsive to the election of claims of Group II (claims 9–16) made by telephone interview between the undersigned and Examiner Nguyen on April 2, 2001, please amend the above-identified patent application as follows.

IN THE CLAIMS:

Please cancel claims 1–8 and 16–21 without prejudice to further prosecution in a divisional, continuation, continuation-in-part, or other related patent application. The cancellation of these claims is made solely to comply with the Examiner's imposition of a Restriction and in no way implies the invention(s) defined by the cancelled claims is (are) unpatentable.

Please amend claim 9 as follows.

9. (Amended) A composition useful for inhibiting expression of a target gene in a subject, comprising a chimeric oligonucleotide [as recited in claim 1] having the structure:

wherein:W represents a 5'-O-alkyl nucleotide;each of X¹ and X² represents a block of seven to twelve phosphodiester-linked 2'-O-alkyl ribonucleotides;Y represents a block of five to twelve phosphorothioate-linked deoxyribonucleotides; and

Chiron Docket No.: PP01565.002

Serial No.: 09/648.254

Page 1 of 6

Z represents a blocking group effective to block nuclease activity at the 3' end of the oligonucleotide

in a pharmaceutically acceptable vehicle.

REMARKS

The Applicants acknowledge the election of Group II, claims 9-15, without traverse. The undersigned thanks the Examiner for the courtesies extended in the telephone interview of April 2, 2001.

Claims 9-15 are pending in the present application. Claims 1-8 and 16-21 have been cancelled without prejudice to further prosecution in a divisional, continuation, continuation-in-part, or other related patent application. The cancellation of these claims is made solely to comply with the Examiner's imposition of a Restriction and in no way implies the invention(s) defined by the cancelled claims is (are) unpatentable.

CONCLUSION

In view of the foregoing, it is respectfully submitted that the above-identified patent application is in condition for allowance. A Notice of Allowance is therefore respectfully requested. The Examiner is encouraged to contact the undersigned at the telephone number or e-mail address provided below to resolve any remaining questions or issues.

Respectfully submitted,
CHIRON CORPORATION



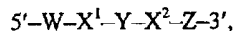
David P. Lentini
Registration No. 33,944

David P. Lentini
CHIRON CORPORATION
4560 Horton Street, M/S R440
Emeryville, CA 94608-2916
Tel.: (510) 923-2706
Fax: (510) 655-3542
E-mail: david_lentini@cc.chiron.com

Chiron Docket No.: PP01565.002
Serial No.: 09/648,254
Page 2 of 6

Claims Pending in U.S. Patent Application Serial No. 09/648,245

9. A composition useful for inhibiting expression of a target gene in a subject, comprising a chimeric oligonucleotide having the structure:



wherein:

W represents a 5'-O-alkyl nucleotide;

each of X^1 and X^2 represents a block of seven to twelve phosphodiester-linked 2'-O-alkyl ribonucleotides;

Y represents a block of five to twelve phosphorothioate-linked deoxyribonucleotides; and

Z represents a blocking group effective to block nuclease activity at the 3' end of the oligonucleotide

in a pharmaceutically acceptable vehicle.

10. The composition of claim 9, wherein the vehicle includes a lipid-cationic peptoid conjugate of the formula:



where

L is selected from a lipid moiety comprising at least one fatty alkyl or alkenyl chain between about 8 and 24 carbon atoms in length and a steroid;

each group R is independently selected from alkyl, aminoalkyl, and aralkyl, and

the linker is selected from the group consisting of a direct bond, an oligopeptide, a substantially linear alkyl chain from 2 to about 30 bonds in length, and a substantially linear chain from 2 to about 30 bonds in length consisting of alkyl bonds and one or more linkages selected from the group consisting of ester, amide, carbonate, carbamate, disulfide, peptide, and ether.

11. The composition of claim 10, wherein the linker is from 3 to about 15 bonds in length.

12. The composition of claim 10, wherein said fatty alkyl or alkenyl chain is between about 14 and 24 carbon atoms in length.

13. The composition of claim 10, wherein L is a phospholipid group, having two fatty alkyl or alkenyl chains between about 8 and 24 carbon atoms in length.

14. The composition of claim 10, wherein L is a cholesteryl group.

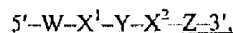
15. The composition of claim 10, wherein R is isopropyl or 4-methoxyphenyl.

Redline Comparison of Claims Pending and Filed

~~1. A chimeric oligonucleotide having the formula 5'-W-X¹-Y-X²-Z-3', where~~

~~W represents a 5'-O-alkyl nucleotide;~~

~~9. A composition useful for inhibiting expression of a target gene in a subject, comprising a chimeric oligonucleotide having the structure:~~



~~wherein:~~

~~W represents a 5'-O-alkyl nucleotide;~~

~~—each of X¹ and X² represents a block of seven to twelve phosphodiester-linked 2'-O-alkyl-2'-O-alkyl ribonucleotides;~~

~~—Y represents a block of five to twelve phosphorothioate-linked deoxyribonucleotides; and~~

~~Z represents a blocking group effective to block nuclease activity at the 3'-3' end of the oligonucleotide.~~

~~-oligonucleotide~~

~~2. The oligonucleotide of claim 1, wherein the alkyl groups of the 5'-O-alkyl nucleotide and the 2'-O-alkyl ribonucleotides are lower alkyl groups.~~

~~3. The oligonucleotide of claim 2, wherein the alkyl groups of the 2'-O-alkyl ribonucleotides are methyl groups.~~

~~4. The oligonucleotide of claim 1, wherein the 5'-O-alkyl nucleotide is a 5'-O-alkyl thymidine.~~

~~5. The oligonucleotide of claim 1, wherein the 5'-O-alkyl nucleotide is linked to X¹ via a phosphodiester linkage or a phosphorothioate linkage.~~

~~6. The oligonucleotide of claim 1, wherein group Z is linked to X² via a linkage selected from the group consisting of a phosphotriester linkage, a phosphorothioate linkage, and a phosphoramidate linkage.~~

~~7. The oligonucleotide of claim 1, wherein Z is a 3'-to-3' linked nucleotide.~~

~~8. The oligonucleotide of claim 1, wherein the segment X¹-Y-X² has a nucleotide sequence selected from the group consisting of SEQ ID-NOs: 1-24.~~

~~9. A composition useful for inhibiting expression of a target gene in a subject, comprising a chimeric oligonucleotide as recited in claim 1 in a pharmaceutically acceptable vehicle.~~

~~10. The composition of claim 9, wherein the vehicle includes a lipid-cationic peptoid conjugate of the formula:~~

Chiron Docket No.: PP01565.002

Serial No.: 09/648,254

Page 4 of 6

$L\text{-linker-[N(CH}_2\text{CH}_2\text{NH}_2\text{)CH}_2\text{(C=O)-N(CH}_2\text{CH}_2\text{R)CH}_2\text{(C=O)-N(CH}_2\text{CH}_2\text{R)CH}_2\text{(C=O)]}_3\text{-NH}_2$

where

— L is selected from a lipid moiety comprising at least one fatty alkyl or alkenyl chain between about 8 and 24 carbon atoms in length and a steroid;

— each group R is independently selected from alkyl, aminoalkyl, and aralkyl, and

— the linker is selected from the group consisting of a direct bond, an oligopeptide, a substantially linear alkyl chain from 2 to about 30 bonds in length, and a substantially linear chain from 2 to about 30 bonds in length consisting of alkyl bonds and one or more linkages selected from the group consisting of ester, amide, carbonate, carbamate, disulfide, peptide, and ether.

11. The composition of claim 10, wherein the linker is from 3 to about 15 bonds in length.

12. The composition of claim 10, wherein said fatty alkyl or alkenyl chain is between about 14 and 24 carbon atoms in length.

13. The composition of claim 10, wherein L is a phospholipid group, having two fatty alkyl or alkenyl chains between about 8 and 24 carbon atoms in length.

14. The composition of claim 10, wherein L is a cholesteryl group.

15. The composition of claim 10, wherein R is isopropyl or 4-methoxyphenyl.

16. The composition of claim 10, wherein the lipid-cationic peptoid conjugate is of the formula:

$L\text{-(CH}_2\text{)}_n\text{-(C=O)-[N(CH}_2\text{CH}_2\text{NH}_2\text{)CH}_2\text{(C=O)-N(CH}_2\text{CH}_2\text{R)CH}_2\text{(C=O)-N(CH}_2\text{CH}_2\text{R)CH}_2\text{(C=O)]}_3\text{-NH}_2$,

where

— L is selected from (i) a phosphatidylethanolamine group, having fatty alkyl or alkenyl chains between about 8 and 24 carbon atoms in length, and (ii) a cholesteryl group linked to the adjacent $\text{-(CH}_2\text{)}_n\text{-}$ segment by an ester, amide or carbamate linkage;

— n is 1-5; and

— R is selected from isopropyl and 4-methoxyphenyl.

17. The composition of claim 16, wherein the lipid-cationic peptoid conjugate is selected from the group consisting of compounds represented herein as:

(a) Lipitoid 1, or DMPE(NaeNmpeNmpe)₂;

(b) Lipitoid 2, DMPE(NaeNiaNia)₂;

(c) Cholesterol 1, or Chol-β-ala-(NaeNmpeNmpe)₂;

(d) Cholesterol 2, or Chol-Ahx-(NaeNmpeNmpe)₂;

(e) Cholesterol 3, or Chol-β-ala-(NaeNiaNia)₂; and

Chiron Docket No.: PP01565.002

Serial No.: 09/648,254

Page 5 of 6

(f) Cholesterol 4, or Chol-Ahx (NacNiaNia)₃.

~~18. A method of inhibiting expression of a target gene in a subject, comprising
administering to the subject, in a pharmaceutically acceptable vehicle, an amount of a chimeric
oligonucleotide as recited in claim 1 which is effective to specifically hybridize to all or part of a selected
target nucleic acid sequence derived from the gene.~~

~~19. The method of claim 18, wherein the target nucleic acid sequence is a mRNA derived from the
target gene.~~

~~20. The method of claim 19, wherein the segment X¹-Y-X² of the chimeric oligonucleotide has a
nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-24.~~

~~21. The method of claim 18, wherein the vehicle includes a lipid-cationic peptoid conjugate as recited
in claim 11.~~